DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA#: 20-796

CHEMISTRY REVIEW: #1

DATE REVIEWED: 13-Jul-98

Submission Type	Letter Date	CDER Stamp Date	Analaus a a
ORIGINAL RESUBMISSION N(BC) - EA/categorical exclusion N(BC) - packaging site AMENDMENT	24-OCT-97 23-DEC-07	24-OCT-97 24-DEC-97 27-APR-98 04-MAY-98 11-MAY-98	Assigned Date [Assigned Date] 27-APR-98 05-MAY-98

NAME AND ADDRESS OF APPLICANT:

Orion Corporation P.O. Box 65

Fin-02101 Espoo, Finland

DRUG PRODUCT NAME:

Proprietary:

COMTAN®

Ncnproprietary/Established/USAN: entacapone [INN, USAN name is pending]

Code Name/#:

OR-611

Chem. Type/Therapeutic Class:

DESI/PATENT STATUS: US Patent Nos. 5,446,194 (expiry 8/29/2012), 5,135,950 (expiry 10/31/2010)

4,963,590 (expiry 11/27/2007) and 5,112,861 (expiry 5/12/20090)

PHARMACOLOGICAL CATEGORY / INDICATION:

Parkinson's disease, adjunct to levodopa/dopa therapy

DOSAGE FORM:

Tablets

STRENGTH(S): ROUTE OF ADMINISTRATION:

200 mg Oral

DISPENSED:

XX Rx

SPECIAL PRODUCTS:

OTC

CHEMICAL NAME, STRUCTURAL FORMULA AND MOLECULAR FORMULA:

(E)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethyl-2-propenamide (CAS) (E)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethylacrylamide (IUPAC)

CAS No. 130929-57-6

Mol. Formula: C₁₄H₁₅N₃O₅

Mol. Weight: 305.29

SUPPORTING DOCUMENTS: DMF/

RELATED DOCUMENTS: IND

CONSULTS: Tradename consulted to nomenclature committee on 30-OCT-97, no recommendation available.

REMARKS / COMMENTS: /

Most are relatively minor and could be resolved quickly.

Establishment evaluations requested on 03-MAR-98. Initial site inspections are complete, with field/compliance recommendations still pending. Methods Validation will not be initiated until all deficiencies in analytical method and validation have been addressed by the sponsor.

CONCLUSIONS AND RECOMMENDATIONS:

Recommend Information Request letter to sponsor.

cc: Orig. NDA [NDA Number] 20796

HFD-120/Division File

HFD-120/MHeimann HFD-120/TWheelous

HFD-120/MGuzewska/R/D Init. by

HFD-810/CHoibera

Martha R. Heimann, Ph.D., Review Chemis Filename:

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

Revie	ew of Chemistry	, Manufactur	ing, and Controls	
NDA#: 20-796	CHEMISTRY RI		*	DATE REVIEWED: 11-Dec-98
Submission Type	Letter Date	, cr	DER Stamp Date	
N(BC) N(BC) N(BL) N(BC) – Method validation package	30-SEP-98 11-NOV-98 24-NOV-98 02-DEC-98	01- 13- 25-	-OCT-98 -NOV-98 -NOV-98 -DEC-98	01-OCT-98 13-NOV-98 25-NOV-98
NAME AND ADDRESS OF APPLICANT:	Orion Cor	poration 35, Fin-02101		03-NOV-98
DRUG PRODUCT NAME: Proprietary: Nonproprietary/Established/US/ Code Name/#: Chem. Type/Therapeutic Class: DESI/PATENT STATUS: US Patent N	COMTAN [®] AN: entacapon OR-611 1 S	e [USAN lette		
DESI/PATENT STATUS: US Patent N 4,963,590 (expiry 11/27/2007) and 5	.112.861 (expir	expiry 8/29/20 y-5/12/2009)	012), 5,135,950 <u>(</u>	expiry 10/31/2010).
PHARMACOLOGICAL CATEGORY / INDIC DOSAGE FORM: STRENGTH(S): ROUTE OF ADMINISTRATION: DISPENSED: SPECIAL PRODUCTS:	Ta 200 Ora X)	olets 0 mg al <u>C_Rx</u>	ease, adjunct to le	evodopa/dopa therapy
CHEMICAL NAME, STRUCTURAL FORML	No			
(E)-2-Cyano-3-(3,4-dihydroxy-5-nitro) (E)-2-Cyano-3-(3,4-dihydroxy-5-nitro) CAS No. 130929-57-6 Mol. Formula: C ₁₄ H ₁₅ N ₃ O ₅ Mol. SUPPORTING DOCUMENTS:	phenyl)-N,N-die phenyl)-N,N-die Weight: 305,29	thylacrylamid	e (IUPAC)	HO CH ₃ HO CH ₃
RELATED DOCUMENTS: IND	offensylver and other and a second of the se	· · · · · · · · · · · · · · · · · · ·	<i></i>	
CONSULTS: Tradename consult was re	turned by Nom	ondeter in		
REMARKS / COMMENTS: Deficiencies is	lentified in NO	Circiature cor	nmittee on 23-FE	B-98 - Acceptable
Establish			The same of the sa	ble overall compliance
recommendation dated 04-AUG-1998. being initiated.	LANSED METU	ods validation	is adequate and	methods validation is
CONCLUSIONS AND RECOMMENDATIONS	<u>.</u>			
Recommend approval. Action letter ne should be reviewed when submitted.		ethod validat	ion statement an	d final container labeling
cc: Orig. NDA 20-768 HFD-120/Division File HFD-120/MHeimann HRD-120/TWheelous? HFD-120/MGuzewska/R/D Init. by:-MG)2.H.98	Martha R. Heir Filename: D:\\	nann, Ph.D., Revie WORD#WP\#NDA\	/2/1/98 w Chemist N20-796\N20-796.002.DOC

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DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS

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Review of Chemistry,	Manufacturing,	and (Controls
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NDA#: 20-796	CHEMISTRY REVIEW	: #3 D	ATE REVIEWED: 21-SEP-99
Submission Type	Letter Date	CDER Stamp Date	Assigned Date
N(BC)	25-MAY-99	26-MAY-99	27-MAY-99
NAME AND ADDRESS OF APPLICANT:	Orion Corporat P.O. Box 65, Fi Espoo, Finland	ion in-02101	27-1010-1-23
DRUG PRODUCT NAME: Proprietary: Nonproprietary/Established/US Code Name/#: Chem. Type/Therapeutic Class:	OR-611	SAN letter dated 27-AUG-97	7]
DESI/PATENT STATUS: US Patent N 4,963,590 (expiry 11/27/2007) and	Nos. 5,446,194 (expir 5,112,861 (expiry 5/1	y 8/29/2012), 5,135,950 (ex 12/2009)	piry 10/31/2010),
PHARMACOLOGICAL CATEGORY / IND DOSAGE FORM: STRENGTH(S): ROUTE OF ADMINISTRATION: DISPENSED: SPECIAL PRODUCTS:	ICATION: Parkins Tablets 200 mg Oral XX R	İ	odona/dopa therapy
CHEMICAL NAME, STRUCTURAL FORM	IULA AND MOLECULAR	R FORMULA:	
(E)-2-Cyano-3-(3,4-dihydroxy-5-nitr (E)-2-Cyano-3-(3,4-dihydroxy-5-nitr CAS No. 130929-57-6 Mol. Formula: C ₁₄ H ₁₅ N ₃ O ₅ Mo SUPPORTING DOCUMENTS:	ophenyl)-N,N-diethyl ophenyl)-N,N-diethyl I. Weight: 305.29	-2-propenamide (CAS) не acrylamide (IUPAC) не	CN N CH ₃
CONSULTS: Tradename consult was REMARKS / COMMENTS:	returned by Nomeno	clature committee on 23-FEE	8-98 - Acceptable
CONCLUSIONS AND RECOMMENDATION CMC information is adequate to sup standard method validation stateme cc: Orig. NDA 20-768 HFD-120/Division File HFD-120/MHeimann HFD-120/TWheelous	port approvat of the part and final container	labeling should be reviewed	d when submitted.
	Ma MG File	ntha R. Heimann, Ph.D., Review ename: D:\WORD#WP\#NDA\	9/2//99 w Chemist N20-796\N20-796.003.DOC

HFD-810/JSimmons